सत्यमेव जयते

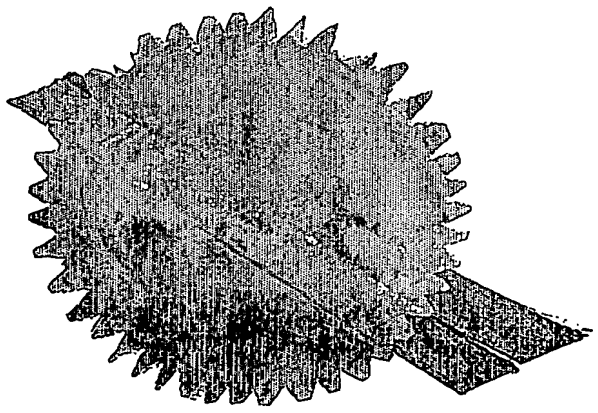
INTELLECTUAL PROPERTY INDIA

GOVERNMENT OF INDIA
MINISTRY OF COMMERCE & INDUSTRY,
PATENT OFFICE, DELHI BRANCH,
W - 5, WEST PATEL NAGAR,
NEW DELHI - 110 008.

PRIORITY DOCUMENT
SUBMITTED OR TRANSMITTED IN COMPLIANCE WITH RULE 17.1(a) OR (b)

I, the undersigned being an officer duly authorized in accordance with the provision of the Patent Act, 1970 hereby certify that annexed hereto is the true copy of the ***Application*** *and* ***Complete Specification*** *filed in connection with Application for Patent No.* ***1154/Del/02*** *dated* ***15th November 2002.***

Witness my hand this 22nd day of March 2004.



(S.K. PANGASA)
Assistant Controller of Patents & Designs

1154 DEL 02

15 NOV 2002

FORM 1

THE PATENTS ACT, 1970
(39 of 1970)

APPLICATION FOR GRANT OF A PATENT

(See Sections 7, 54 and 135 and rule 33A)

1 We, **RANBAXY LABORATORIES LIMITED,** a Company incorporated under the Companies Act, 1956, Corporate Office at 19, Nehru Place, New Delhi - 110 019, India

2. hereby declare –

(a) that we are in possession of an invention titled " **BIGUANIDE-SULFONYL UREA COMBINATIONS FOR DIABETES** "

(b) that the Complete Specification relating to this invention is filed with this application.

(c) that there is no lawful ground of objection to the grant of a patent to us.

3. Further declare that the inventors for the said invention are

a. SUMIT MADAN

b. ANUPAM TREHAN

c. VINOD KUMAR ARORA

d. RAJIV MALIK

DUPLICATE

of Ranbaxy Laboratories Limited, Plot No. 20, Sector-18, Udyog Vihar Industrial Area, Gurgaon – 122001 (Haryana), India,

all Indian Nationals.

4. That we are the assignee or legal representative of the true and first inventors.

5. That our address for service in India is as follows:

DR. B. VIJAYARAGHAVAN
Associate Director – Intellectual Property
Ranbaxy Laboratories Limited
Plot No.20, Sector – 18,
Udyog Vihar Industrial Area,
Gurgaon – 122001 (Haryana).
INDIA.
Tel. No. (91-124) 6342001 – 10
Fax No. (91-124) 6342027

6. Following declaration was given by the inventors in the convention country:

We, SUMIT MADAN, ANUPAM TREHAN, VINOD KUMAR ARORA, RAJIV MALIK of Ranbaxy Laboratories Limited, Plot No. 20, Sector – 18, Udyog Vihar Industrial Area, Gurgaon–122001 (Haryana), India, all Indian Nationals, the true and first inventors for this invention in the convention country declare that the applicants herein, **Ranbaxy Laboratories Limited**, 19, Nehru Place, New Delhi - 110 019, India, is our assignee or legal representative.

a. Sumit Madan

(SUMIT MADAN)

b. Anupam Trehan

(ANUPAM TREHAN)

c.

(VINOD KUMAR ARORA)

d.

(RAJIV MALIK)

7. That to the best of our knowledge, information and belief the fact and matters stated herein are correct and that there is no lawful ground of objection to the grant of patent to us on this application.

8. Followings are the attachment with the application:

a. Complete Specification (3 copies)

b. Drawings (3 copies)

c. Statement and Undertaking on FORM – 3

d. Fee Rs.5,000/- (Rupees Five Thousand only..) in cheque bearing No. **684623** dated **23.09.2002** on **ANZ Grindlays Bank, New Delhi.**

We request that a patent may be granted to us for the said invention.

Dated this 5TH day of **November**, 2002.

For Ranbaxy Laboratories Limited

Vinay Kumar Kaul

RANBAXY LABORATORIES LTD. N. Delhi

(SUSHIL KUMAR PATAWARI)
Company Secretary

1154 DEL 02

15 NOV 2002

FORM 2

The Patents Act, 1970

(39 of 1970)

COMPLETE SPECIFICATION
(See Section 10)

BIGUANIDE – SULFONYUREA COMBINATIONS FOR DIABETES

RANBAXY LABORATORIES LIMITED
19, NEHRU PLACE, NEW DELHI - 110019

A Company incorporated under the Companies Act, 1956.

The following specification particularly describes and ascertains the nature of this invention and the manner in which it is to be performed:

The present invention relates to a novel pharmaceutical composition for oral administration of combination of antidiabetic agents wherein one is present in an extended release form and the other in an immediate release form.

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia, insulin resistance, and is often associated with other disorders such as obesity, hypertension, hyperlipidemia, as well as complications such as cardiovascular disease, retinopathy, neuropathy, and nephropathy. The disease is progressive in nature, and can often be controlled initially by diet alone, but generally requires treatment with drugs or injections of exogenous insulin.

Sulfonylureas are a group of drugs that induce hypoglycemia by stimulating insulin release from the pancreas. Suitable sulfonylureas include acetohexamide, glibenclamide (glyburide), glipizide, gliclazide, glimepiride, tolazamide and tolbutamide. Glyburide is available as tablets of 1.25mg, 2.5mg and 5mg strengths for oral administration and is administered twice a day. Glipizide tablets are available in 5 and 10mg tablets. Similarly, glimepiride is available as 1, 2 and 4 mg tablets to be administered once daily.

Biguanides are another group of drugs that have been widely used as antidiabetics. They act by increasing insulin activity in peripheral tissues, reducing hepatic glucose output due to inhibition of gluconeogenesis and reducing the absorption of glucose from the intestine. Metformin, phenformin, buformin, etc. belong to this group. Metformin has been widely prescribed for lowering blood glucose in patients with non-insulin-dependent diabetes (NIDDM), marketed in 500, 850 or 1000mg strengths. However, being a short acting drug, metformin requires twice-daily or three-times-a-day dosing (500 - 850 mg tab 2-3x/day or 1000 mg bid with meals).

Unlike the sulfonylureas, biguanides do not induce release of insulin from the pancreas. Its effects are mediated by increasing insulin activity in peripheral tissues, reducing hepatic glucose output due to inhibition of gluconeogenesis and reducing the absorption of glucose from the intestine.

These agents are often given in combination with drugs that increase the output of insulin from the pancreas, such as the sulfonylureas, which sometimes result in greater efficacy and/or the ability to use lower doses of the drugs, with an improved side effect profile. Adverse events associated with the administration of biguanides are anorexia, nausea, vomiting and diarrhea, etc. The adverse events may be partially avoided by either reducing the initial and / or maintenance dose using an extended-release dosage form. Another advantage of an extended-release dosage form is a reduction in the frequency of administration. Findings suggest that extended-release dosage form of a biguanide may improve the quality of therapy in patients with NIDDM.

Studies have shown that a combination of insulin secretion enhancers and insulin senstivity enhancer has a remarkable effect on glycemic control. The different mechanism of action in targeting hyperglycemia are complimentary and capable of providing remedy for both the deficiency in insulin secretion and insulin sensitivity conditions.

The combination therapy therefore plays an important therapeutic role, since it allows obtaining an effective metabolic control in NIDDM patients in whom the therapy with only sulfonylureas or only biguanides becomes ineffective with time.

Although extended-release formulations of biguanide alone, as well as biguanide (conventional) in combination with sulfonylureas are well known now, but no such formulation is available which can provide the combined benefits of biguanide once daily and sulfonylureas in once per day dosage form. This combination administered in a single dosage form for once daily administration will not only improve patient compliance but also save time and cost for preparing two different dosage forms.

In the present invention we have found that a combination of a sulfonylurea as immediate release form and a biguanide as extended release form, administered once daily provide equivalent efficacy when compared to an extended release biguanide and sulfonylurea in separate dosage forms administered together.

Therefore, the present invention is related to a novel pharmaceutical composition for oral administration, comprising a combination of a biguanide and a sulfonylurea, wherein the biguanide is present as extended release form and the sulfonylurea is present as immediate release form in a single dosage form.

The invention provides a dosage form containing both sulfonylurea and biguanide. The sulfonylurea is contained in an immediate-release form, so that it is released substantially immediately upon ingestion (i.e. upon swallowing). Generally at least 80% of the sulfonylurea is released from the dosage form within an hour after administration. The biguanide, by contrast, releases in a sustained fashion, at least about 75% of the drug contained in the dosage form releasing over a period of 4 to 36 hours, preferably about 8 to 24 hours. The term "about" as used above and elsewhere herein means plus or minus 10% for each of the numerical limits.

Biguanide as employed herein is intended to include metformin, phenformin, buformin and the like.

Sulfonylurea as employed herein is intended to include acetohexamide, glibenclamide (glyburide), glipizide, gliclazide, glimepiride, tolazamide, tolbutamide and the like.

The pharmaceutical compositions of the present invention can be administered orally in the form of tablets such as coated tablets or bilayered tablets; or in form of capsules containing pellets, beads, granules, multiparticulates, tablets or powder.

A sulfonylurea can be incorporated into the dosage form as an immediate release component in a variety of ways. For example, it can be incorporated into an exterior coating for a tablet from which it releases substantially immediately upon ingestion. Such a coating can similarly be applied to each of the particles comprising a multiparticulate i.e. granules, beads. If the dosage form is to be a capsule, sulfonylurea can be contained in a single pellet inside the capsule from which it releases substantially immediately once the capsule shell dissolves. Alternatively, the sulfonylurea can be contained in several smaller pellets or be present as immediate release particles or as immediate release layer over the extended release cores or beads. The coating

composition may comprise water-soluble polymers such as polyvinyl pyrrolidone, hydroxypropyl cellulose, polyvinyl alcohol, hydroxypropyl methylcellulose and the like. The polymer may be applied as a solution in an organic solvent or as an aqueous dispersion. The solvent may be selected from water; alcohols like ethyl alcohols or isopropyl alcohol; ketones like acetone, or ethylmethyl ketone; chlorinated hydrocarbons like dichloromethane and trichloroethane. The coating composition may also comprise plasticizers, opacifiers and colorants. Any conventional coating equipment may be employed to facilitate coating such as centrifugal fluidized bed coating apparatus, pan coating apparatus, or fluidized bed granulating coating apparatus.

Due to poor dispersibility in solvents, the coating composition comprising the sulfonylurea may also include a wetting agent. Suitable wetting agents for use in conjunction with the present invention include hydrophilic and hydrophobic surfactants. Hydrophilic surfactants may be selected from the group consisting of hydrophilic non-ionic surfactants, hydrophilic ionic surfactants, and combinations thereof. Hydrophobic surfactant may be selected from the group consisting of alcohols; polyoxyethylene alkylethers; fatty acids; glycerol fatty acid monoesters; glycerol fatty acid diesters; acetylated glycerol fatty acid monoesters; acetylated glycerol fatty acid diesters, lower alcohol fatty acid esters; polyethylene glycol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polypropylene glycol fatty acid esters; polyoxyethylene glycerides; lactic acid derivatives of monoglycerides; lactic acid derivatives of diglycerides; propylene glycol diglycerides; sorbitan fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers, polyethyleneglycols as esters or ethers, polyethoxylated castor oil; polyethoxylated hydrogenated castor oil, polyethoxylated fatty acid from castor oil or polyethoxylated fatty acid from castor oil or polyethoxylated fatty acid from hydrogenated castor oil.

The biguanide may be incorporated in an extended release core by dispersing in a rate controlling polymer matrix; or biguanide may be layered onto pharmaceutically acceptable inert cores or seeds, which is surrounded by rate controlling polymer layer.

The term matrix, as used herein, refers to a uniform mixture of a biguanide, rate-controlling polymers and optionally other excipients. The rate-controlling polymers may be hydrophilic, hydrophobic or a combination thereof. The rate-controlling polymers are uniformly dispersed throughout the matrix to achieve uniform drug release. Hydrophilic polymers of the present invention include cellulose derivatives such as hydroxypropylcellulose, hydroxypropyl methylcellulose, hydroxyethylcellulose, hydroxymethylcellulose, carboxymethylcellulose, methylcellulose, sodium carboxymethylcellulose or combinations thereof. The hydrophobic polymers may be selected from poly (ethylene) oxide, ethyl cellulose, cellulose acetate, cellulose acetate butyrate, hydroxypropyl methylcellulose phthalate, poly (alkyl) methacrylate, and copolymers of acrylic or methacrylic acid esters, waxes, shellac and hydrogenated vegetable oils.

In addition to the active and rate-controlling polymers, the matrix of the present invention may contain other pharmaceutically acceptable excipients, which act in one or more capacities as diluents, binders, lubricants, glidants, colorants or flavoring agents. The matrix may be made by any pharmaceutically acceptable technique that achieves uniform blending, e.g. dry blending, wet granulation, compaction and fluid bed granulation.

Suitable diluents include pharmaceutically acceptable inert fillers such as microcrystalline cellulose, lactose, dibasic calcium phosphate, mannitol, starch, sorbitol, sucrose, dextrose, maltodextrin or mixtures thereof.

Suitable binders may be selected from polyvinyl pyrrolidone, lactose, starches, gums, waxes, gelatin, polymers or mixtures thereof.

Suitable lubricants include colloidal silicon dioxide, talc, stearic acid, magnesium stearate, magnesium silicate, polyethylene glycol, sodium benzoate, sodium lauryl sulphate, fumaric acid, zinc stearate, paraffin, or mixtures thereof.

Suitable glidants may be selected from talc and colloidal silicon dioxide.

The matrix formed can be compressed to form the tablets.

Beads or pellets can be prepared using techniques like extrusion-spheronization, drug layering, granulation and the like. The inert core or seeds may be water soluble like sucrose, lactose, maltodextrin and the like or water insoluble like microcrystalline cellulose, partially pregelatinized starch, dicalcium phosphate and the like. Biguanide and rate controlling polymer can be coated as single layer or as separate layers on to these inert cores; or granulated with the inert cores; or mixed with inert cores and extruded and spheronized to form the pellets.

The coating can be applied to the inert/active core using a conventional coating pan or a spray coater, or a rotating perforated pan or an automated system, a fluidized bed process or any other suitably automated coating equipment.

The extended-release core containing biguanide may optionally be coated to seal the core. The coated active cores may be dried under conditions effective for drying e.g. in an oven or in a fluidized bed dryer.

Finally beads/pellets comprising extended release and immediate release portions can be filled into capsules or compressed to form the tablets.

The present invention is further illustrated by the following examples. Those skilled in the art will find it apparent that various modifications and variations can be made to the formulations of this invention.

EXAMPLE 1

	INGREDIENTS	Mg/tablet
CORE	Metformin Hydrochloride	500
	Microcrystalline Cellulose	245
	Sodium Carboxymethyl Cellulose	150
	Purified Water	q.s.
	Hydroxypropyl methylcellulose	100
	Magnesium Stearate	5
SEAL COAT	Hydroxypropyl methylcellulose E5	15.6
	Polyethylene glycol 4000	4.8
	Titanium Dioxide	2.4
	Talc	1.2
	Purified Water	q.s.
ACTIVE COAT	Glimepiride (20% extra to compensate for losses)	1.2
	Caprylocaporyl Macrogolglycerides	14.4
	Hydroxypropyl methylcellulose E5	29.35
	Polyethylene glycol 4000	8.6
	Titanium Dioxide	4.3
	Talc	2.15
	Purified Water	q.s.

Procedure:

1. Metformin hydrochloride was milled through 1 mm screen and mixed with microcrystalline cellulose and sodium carboxymethyl cellulose. The blend was sieved through No. 44 mesh, transferred to Rapid mixer granulator and wet granulated with purified water. The granules were dried in Fluid bed dryer, sized through multimill and sifted through No. 30 mesh.
2. Hydroxypropyl methylcellulose was separately sifted through No.30 mesh and mixed with granules in a low shear mixer. The blend was then mixed with magnesium stearate and compressed into tablets.
3. A coating dispersion was prepared by dispersing all ingredients of seal coat in water. The tablets were coated with this dispersion till weight build up of 2% w/w.
4. To prepare the active coat, caprylocaproyl monoglyceride was dissolved in purified water. To this solution, glimepiride was added with stirring to form dispersion. The other ingredients of the active coat were added with stirring to this dispersion and the resulting dispersion was

then coated upon the tablets obtained from step 3, using spray-coating, up to a weight build up of 5% w/w.

EXAMPLE 2

	INGREDIENTS	Mg/tablet
CORE	Metformin Hydrochloride	500
	Microcrystalline Cellulose	245
	Sodium Carboxymethyl Cellulose	150
	Hydroxypropyl methylcellulose	100
	Magnesium Stearate	5
SEAL COAT	Hydroxypropyl methylcellulose E5	15.6
	Polyethylene glycol 4000	4.8
	Titanium Dioxide	2.4
	Talc	1.2
	Purified Water	q.s.
ACTIVE COAT	Glimepiride (20% extra to compensate for losses)	1.2
	Caprylocaporyl Macrogolglycerides	14.4
	Hydroxypropyl methylcellulose E5	29.35
	Polyethylene glycol 4000	8.6
	Titanium Dioxide	4.3
	Talc	2.15
	Purified Water	q.s.

Procedure:

1. Metformin hydrochloride was milled through 1 mm screen and mixed with microcrystalline cellulose and sodium carboxymethyl cellulose. The blend was sieved through No. 44 mesh.
2. Hydroxypropyl methylcellulose was separately sifted through No.30 mesh and mixed with the blend in a low shear mixer. The blend was then mixed with magnesium stearate and compressed into tablets.
3. A coating dispersion was prepared by dispersing all ingredients of seal coat in water. The tablets were coated with this dispersion till weight build up of 2 w/w%.
4. To prepare the active coat, caprylocaproyl monoglyceride was dissolved in purified water. To this solution, glimepiride was added with stirring to form dispersion. The other

ingredients of the active coat were added with stirring to this dispersion and the resulting dispersion was then coated upon the tablets obtained from step 3, using spray-coating, up to a weight build up of 5% w/w.

EXAMPLE 3

	INGREDIENTS	Mg/tablet
CORE	Metformin Hydrochloride	500
	Microcrystalline Cellulose	245
	Sodium Carboxymethyl Cellulose	150
	Hydroxypropyl methylcellulose	100
	Magnesium Stearate	5
SEAL COAT	Hydroxypropyl methylcellulose E5	15.6
	Polyethylene glycol 4000	4.8
	Titanium Dioxide	2.4
	Talc	1.2
	Purified Water	q.s.
ACTIVE COAT	Glimepiride equivalent to 2 mg (20% extra to compensate for losses)	2.4
	Caprylocaporyl Macrogolglycerides	14.4
	Hydroxypropyl methylcellulose E5	28.15
	Polyethylene glycol 4000	8.6
	Titanium Dioxide	4.3
	Talc	2.15
	Purified Water	q.s.

Procedure:

1. Metformin hydrochloride was milled through 1 mm screen and mixed with microcrystalline cellulose and sodium carboxymethyl cellulose. The blend was sieved through No. 44 mesh.
2. Hydroxypropyl methylcellulose was separately sifted through No.30 mesh and mixed with the blend of step 1 in a low shear mixer. The blend was then mixed with magnesium stearate and passed through roller compactor and then milled again to form granules. These granules are then compressed into tablets.
3. A coating dispersion was prepared by dispersing all ingredients of seal coat in water. The tablets were coated with this dispersion till weight build up of 2% w/w.

4. To prepare the active coat, caprylocaproyl monoglyceride was dissolved in purified water. To this solution, glimepiride was added with stirring to form dispersion. The other ingredients of the active coat were added with stirring to this dispersion and the resulting dispersion was then coated upon the tablets obtained from step 3, using spray-coating, up to a weight build up of 5% w/w.

A comparative dissolution profile of metformin hydrochloride in innovator's marketed tablets (Glucophage XR 500 mg) and tablet formulation made in accordance with the Example 3 was obtained. The dissolution was carried out in USP Apparatus Type I (basket) at a speed of 100 rpm. The medium was 900ml phosphate buffer, pH 6.8. The data obtained is disclosed in Table 1.

Table 1: Comparative in vitro dissolution profile of metformin hydrochloride in Glucophage XR 500 mg vs tablets made in accordance with Example3.

Time (hrs)	Percent release of metformin (%)	
	Glucophage XR tablets	Tablets of Example 3
1	29	28
4	60	64
8	83	91
12	99	100

From the results, it is clearly evident that both the formulations have substantially similar dissolution profiles.

A comparative dissolution profile of glimepiride in innovator's marketed tablets (Amaryl 2 mg) and tablet formulation made in accordance with the Example 3 was obtained. The dissolution was carried out in USP Apparatus Type I at a speed of 100 rpm. The medium was 900ml phosphate buffer, pH 8. The data obtained is disclosed in Table 2.

Table 2: Comparative in vitro dissolution profile of glimepiride in Amaryl 2 mg tablets vs tablets made in accordance with Example 3.

Time (min.)	Percent release of glimepiride (%)	
	Amaryl 2 mg	Tablets of Example 3
15	95	92
30	98	101
45	98	105

From the results, it is clearly evident that more than 95% of the drug is released in 15 minutes and both formulations show substantially similar dissolution profiles.

WE CLAIM:

1. A process for preparing a pharmaceutical composition for oral administration comprising a combination of a biguanide and a sulfonylurea wherein the biguanide is present as extended-release form and the sulfonylurea is present as immediate release form in a single dosage form.

2. A process according to claim 1 wherein the said combination provides mean peak serum concentration and area under the e curve comparable to that obtained for biguanide extended-release and sulfonylurea conventional tablets given together.

3. The process according to claim 1 wherein the biguanide may be selected from metformin, phenformin, buformin and the like.

4. The process according to claim 3 wherein the biguanide is metformin.

5. The process according to claim 1 wherein the sulfonylurea may be selected from acetohexamide, glibenclamide (glyburide), glipizide, gliclazide, glimepiride, tolazamide, tolbutamide and the like.

6. The process according to claim 5 wherein the sulfonylurea is glimepiride.

7. The process according to claim 1 wherein the biguanide is released into said environment of use over a period of 4 to 36 hours.

8. The process according to claim 7 wherein said period is 8 to 24 hours.

9. The process according to claim 1 wherein composition may be administered in the form of tablets or capsules.

10. The process according to claim 9 wherein tablet is a coated tablet.

11. The process according to claim 9 wherein tablet is a bilayered tablet.

12. The process according to claim 9 wherein capsules contains pellets, beads. granules, multiparticulates, tablets or powder.

13. The process according to claim 1 wherein the biguanide is incorporated in an extended-release core.

14. The process according to claim 13 wherein the core comprises a matrix.

15. The process according to claim 14 wherein the matrix comprises a uniform mixture of biguanide and rate controlling polymers.

16. The process according to claim 15 wherein the rate controlling polymers may be hydrophilic, hydrophobic or a combination thereof.

17. The process according to claim 15 wherein the matrix may contain other pharmaceutically acceptable excipients in addition to the biguanide and rate controlling polymers.

18. The process according to claim 17 wherein the pharmaceutically acceptable excipients are selected from diluents, lubricants, binders, glidants, coloring and flavoring agents.

19. The process according to claim 1 wherein the biguanide is layered onto pharmaceutically inert core or seeds.

20. The process according to claim 19 wherein the biguanide layer is further surrounded by rate controlling polymer layer.

21. The process according to claim 19 wherein the inert seeds or core may be water soluble or water insoluble.

22. The process according to claim 1 wherein the sulfonylurea is incorporated into an exterior coating.

23. The process according to claim 22 wherein the coating comprises water-soluble polymers.

24. The process according to claim 23 wherein the coating may contain other pharmaceutical acceptable excipients in addition to the sulfonylurea and water soluble polymers.

25. The process according to claim 24 wherein the pharmaceutically acceptable excipients are selected from wetting agents, plasticizers, opacifiers and colorants.

26. The process according to claim 25 wherein the wetting agents may be selected from hydrophilic and hydrophobic surfactants.

27. The process according to claim 22 wherein the coating is applied to tablets.

28. The process according to claim 22 wherein the coating is applied to granules or beads.

29. The process according to claim 1 wherein the sulfonylurea is present as pellets.

30. A process for preparing a pharmaceutical composition for oral administration comprising a combination of metformin and glimepiride wherein metformin is present as extended-release form and glimepiride is present as immediate release form in a single dosage form.

31. A process according to claim 30 wherein the said combination provides mean peak serum concentration and area under the curve comparable to that obtained for metformin extended-release and glimepiride conventional tablets given together.

Dated this 14TH day of **November, 2002.**

Vinay Kumar Kaul

For Ranbaxy Laboratories Limited

RANBAXY LABORATORIES LTD. N. Delhi

(Sushil Kumar Patawari)
Company Secretary